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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,586	09/11/2003	John P. Leonard	08702.0009-03000	4504

7590 10/05/2004

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,586	LEONARD ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18-25 and 27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,18-25 and 27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 Sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/29/03; 9-11-03 Total 8 sheets
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' preliminary amendment filed October 16, 2003 is acknowledged and has been entered. Claims 1-15, 17 and 26 have been canceled. Claims 16 and 25 have been amended. Claims 16, 18-25 and 27-33 are now pending in the present application.

2. Applicants should update the continuity data on page 1, line 1 of the specification. Application SN 09/512930 is now US Patent 6706264.

3. The use of trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

4. The disclosure is objected to because of the following informalities: see p. 17, l. 3, "and" should be –an--; p. 8, l. 3, "chimerci" should be –chimeric--. Appropriate correction is required.

5. Claims 21-24 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time

the application was filed, had possession of the claimed invention. Claim 21 recites the limitation of "(a) blocks the formation of a heterodimer containing the 40 kD subunit; or (b) allows the formation of a heterodimer containing the 40 kD subunit, but blocks the activity of said heterodimer". Claim 30 recites the limitation of "(a) blocks the formation of a heterodimer containing the 35 kD subunit; or (b) allows the formation of a heterodimer containing the 35 kD subunit, but blocks the activity of said heterodimer". The specification does not set forth any written description of these limitations as now claimed. A review of page 8, line 5 through page 9, line 22 of the specification (as indicated by Applicants, in related applications, to show support for the claim limitations) does not set forth support for the claim limitations. The specification, at pages 8-9, does not set forth a description or enablement for blocking the formation of the heterodimer or allowing the formation of the heterodimer.

6. Claims 16, 18-25 and 27-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a method for treating at least one autoimmune condition in a human subject, said method comprising administering to said subject a therapeutically effective amount of at least one antagonist that binds with a 40 kD subunit of IL-12, wherein said antagonist is chosen from at least one antibody (monoclonal or polyclonal) immunoreactive with the 40 kD subunit and at least one antibody fragment immunoreactive with the 40 kD subunit. Claims also recite the use of an

antagonist that binds with a 35 kD subunit of IL-12 in the same manner. The specification sets forth examples of IL-12 antagonist administration to mice for the treatment of MS (Example 1) and IDDM (Example 2). The specification has not taught such an antagonist or antibody that binds to the 40 kD or 35 kD subunit of the IL-12 that can be used to treat any autoimmune condition (for disease condition see claims 22-24 and 30-33) in a human.

The specification at pages 6-8 appear to be a mere paper protocol for a method of treating autoimmune conditions, for example RA, that administers an antibody that binds to a 40 kD or 35 kD subunit of IL-12 (IL-12 subunit "may be used"; pp. 6-8). Kim et al (2000) teaches that IL-12 levels reflect RA disease activity and that IL-12 is involved in the production of proinflammatory cytokines. An IL-12 blockade (i.e. anti-IL-12 antibodies) could be useful for the treatment of RA. Kim et al also teaches that the IL-12 is composed of the p35 and p40 subunits, but that neither of these (p35 or p40) subunits has been found to display any significant biological function alone (p. 175). Further, Benson et al, 2002 appears to indicate that IL-12 may not have a dominant role in chronic autoimmune diseases but rather IL-23. The IL-12p40 is shared by IL-23, a heterodimeric cytokine. Benson et al found that IL-12 specific neutralization had no beneficial effect on progression of experimental autoimmune encephalomyelitis (EAE), but that neutralization of both IL-12 and IL-23 effectively ameliorated EAE clinical signs. Therefore it is difficult to predict which antibody to the subunits of these cytokines (IL-12 or IL-23) or epitopes of the subunits of these cytokines binding to IL-12 are effective in a method of treating autoimmune diseases, without experimental evidence (see also Fox 2000, p. 237; Becher et al 2002, p. 493).

It is noted that the specification defines "treating" as curing, ameliorating, delaying or preventing onset of, preventing recurrence or relapse of autoimmune conditions or diseases and defines these conditions or diseases (see p. 3, l. 16 to p. 4, l. 3). However, the specification has not set forth enablement for the scope of treating autoimmune conditions as defined by Applicants' specification. Further, the state of the art with regard to preventing autoimmune conditions is unpredictable. There are no known compositions that can be administered to a subject that will prevent an autoimmune condition or disease (multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disease). Adorini teaches that IL-12-dependent Th1 responses have been implicated in a number of experimental autoimmune disorders (IDDM, EAE, collagen-induced arthritis, experimental allergic uveoretinitis, granulomatous colitis, experimental autoimmune myasthenia gravis, and thyroiditis (p. 17, col. 2). Anti-IL-12 mAb treatment prevents superantigen-induced EAE and subsequent replases (p. 17). "These findings suggest that targeting IL-12 may prove beneficial in some forms of MS, and it is likely that IL-12 antagonists can be useful in other autoimmune conditions, such as inflammatory bowel disease. Given the critical role of IL-12 in the induction of Th1-mediated autoimmune diseases, IL-12 antagonists could be candidates for immunointervention." (p. 17). Although Adorini suggests possibility of IL-12 antagonists as candidates for immunointervention, the state of the art has not shown definitively that IL-12 antagonists or antagonists (i.e. antibodies) that bind the 40 kD subunit of IL-12 or 35 kD subunit of IL-12 can be

used to treat or prevent the numerous autoimmune conditions or diseases as claimed by Applicants. The specification does not enable the claimed invention.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 16, 18-22 and 27-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16 and 22 of copending Application No. 09/512701. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim a method of administering to a subject a

therapeutically effective amount of an antibody that binds a 40 kD subunit of IL-12 or 35 kD subunit of IL-12 for the purpose of treating an autoimmune condition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. No claims are allowed.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
September 29, 2004